

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/EP2004/000789

International filing date (day/month/year)  
29.01.2004

Priority date (day/month/year)

International Patent Classification (IPC) or both national classification and IPC  
C12N15/87

Applicant  
BIOSILAB S.R.L

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2004/000789

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2004/000789

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**Box No. II Priority**

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1. ☒ The following document has not been furnished:

☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

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**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	1-3, 5-7, 9-10, 16-23
	No: Claims	4, 8, 11-15, 24-25
Inventive step (IS)	Yes: Claims	1-3, 5-7, 9-10, 16-23
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-25
	No: Claims	

2. Citations and explanations

**see separate sheet**

**Reference is made to the following documents:**

- D1:** Huang and Rubinsky, 2001. Microfabricated electroporation chip for single cell membrane permeabilization. *Sensors and Actuators A*, 89:242.
- D2:** Lin et al. 2003. A microchip for electroporation of primary endothelial cells. *Sensors and Actuators A*, 108:12.

**Introduction**

The present application concerns a biochip for electroporation of single cells. The gist of the application appears to be the possibility to transfer signals to pre-selected single microelectrodes.

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1.1. The prior art does not disclose biochips for electroporation with a control system that permits to transfer signals to pre-selected single microelectrodes. Subject-matter of claims 1-3, 5-7, 9-10 and 16-23 is therefore new (Article 33(2) PCT).

1.2. The problem to be solved by the present invention may be regarded as the electroporation of pre-selected cells. The solution to this problem proposed in claims 1-3, 5-7, 9-10 and 16-23 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

The closest prior art (D1) discloses the electroporation of single cells in a flow through system. In D2 microchips with interdigitating electrodes are disclosed. However, nowhere in the prior art is disclosed the possibility to transfer signals to pre-selected single microelectrodes. The solution put forward in the present application thus allows to electroporate selected single cells instead of just single cells. This selection is neither disclosed nor suggested in D1 or in D2.

2. Claims 4, 8, and 11-15 do not refer to a control system that permits to transfer signals to pre-selected single microelectrodes. Subject-matter, as referred to in said claims is thus not new over D2, where biochips for electroporation with interdigitating electrodes are disclosed.

3. Electroporated cells as referred to in claims 24 and 25 are not new over the prior art, as the method of electroporation does not confer any technical feature specific to said method. The cells are e.g. identical to elctroporated cells disclosed in D1 or D2.

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C. Friedrich